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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte LYNN E. SPITLER and ANTHONY E. MAIDA III

Appeal 2009-004900
Application 08/105,444
Technology Center 1600

Decided: February 24, 2010

Before DONALD E. ADAMS, LORA M. GREEN, and
RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims 1-14 and 21-40, the only claims pending in this application. We have jurisdiction under 35 U.S.C. § 6(b).

STATEMENT OF THE CASE

The claims are directed to a method of inducing an antitumor immune response in a potential or actual prostate tumor-bearing subject (claims 1-7) and a pharmaceutical or veterinary vaccine for eliciting an antitumor immune response to prostate tumors in a subject (claims 8-14 and 21-40). Claims 1 and 8 are illustrative:

1. A method to induce an antitumor immune response in a potential or actual prostate tumor-bearing subject which method comprises administering to said subject a composition comprising an ingredient which is active to induce said immune response and is selected from the group consisting of

at least one antigen over represented in the prostate gland or an immunologically effective portion thereof; and

an expression system capable of generating *in situ* said antigen.

8. A pharmaceutical or veterinary vaccine for eliciting an antitumor immune response to prostate tumors in a subject which comprises an ingredient which is active to elicit said immune response, is formulated for parenteral administration and is

an expression system capable of generating *in situ* an antigen over represented on the prostate gland with respect to other tissues or an immunologically effective portion thereof.

The Examiner relies on the following evidence:

Horoszewicz	US 5,162,504	Nov. 10, 1992
Wright, Jr.	US 5,227,471	Jul. 13, 1993
Israeli et al.	US 5,538,866	Jul. 23, 1996
Spitler	US 5,738,867	Apr. 14, 1998

Andriole et al., *The Diagnosis and Treatment of Prostate Cancer*, 42 ANNU. REV. MED. 9-15 (1991).

Philip M. Arlen and James K. Gulley, *Therapeutic vaccines for prostate cancer: A review of clinical data*, 6 CURRENT OPINION IN INVESTIGATIONAL DRUGS 592-596 (2005).

Ezzell, *Cancer "Vaccines": An Idea Whose Time Has Come?* 7 J. NIH RESEARCH 46-49 (1995)

Hank et al., Chapter 35, Cancer of the Prostate on pages 1073-1113 of Cancer Prinsiples & Practice of Oncology, 4th Edition, edited by DeVita et al., J.B. Lippincott Company, Philadelphia (1993).

Harris et al., *Immunologic Approaches to the Treatment of Prostate Cancer*, 26 SEMINARS IN ONCOLOGY 439-447 (1999).

Hodge et al., *A Recombinant Vaccinia Virus Expressing Human Prostate-Specific Antigen (PSA): Safety and Immunogenicity In A Non-Human Primate*, 63 INT. J. CANCER 231-237 (1995).

Hwnag et al., *Prostate Cancer Vaccines: Current Status*, 26 SEMINARS IN ONCOLOGY 192-201 (1999).

Janis Kuby, Immunology, Second Edition, W.H. Freemen and Company, New York, (1991) pages 590; 613 Tumor-Associated Antigens and Tumor-Specific Antigens.

Dean L. McCarley, M.D. And Roy S. weiner, M.D., *Diagnostic and Therapeutic Utility of Monoclonal Antibodies in Urologic Oncology*, 5 SEMINARS IN SURGICAL ONCOLOGY 293-301 (1989).

Douglas G. McNeel and Miroslav Malkovsky, *Immune-based therapies for prostate cancer*, 96 IMMUNOLOGY LETTER 3-9 (2005).

Meidenbauer et al., *Generation of PSA-Reactive Effector Cells After Vaccination With A PSA-Based Vaccine in Patients With Prostate Cancer*, 43 THE PROSTATE 88-100 (2000).

Williams E. Paul, M.D., Fundamental Immunology, Second Edition, Raven Press, New York, 1989: Differentiation Antigens and Other Tumor-Associated Antigens.

Peshwa et al., *Induction of Prostate Tumor-Specific CD8+ Cytotoxic T-Lymphocytes In Vitro Using Antigen-Presenting Cells Pulsed With Prostatic Acid Phosphatase Peptide*, 36 THE PROSTATE 129-138 (1998).

Michael L. Salgaller, Peptides in Prostate Cancer, Chapter 10, pages 155-171, published by Landes Bioscience (2000).

Lynn E. Spitler, M.D., *Cancer Vaccines: The Interferon Analogy*, 10 CANCER BIOTHERAPY 1-3 (1995).

Webster's Ninth New Collegiate Dictionary, Merriam-Webster Inc. Springfield, MA 1990, 1176; 1290.

Xu et al., *Identification of Differentially Express Genes In Human Prostate Cancer Using Subtraction and Microarray,* 60 CANCER RESEARCH 1677-1682 (2000).

Appellants rely on the following evidence:

Bystryn Declaration, executed October 10, 1996.

Livingston Declaration, executed October 14, 1996.

Mastrangelo Declaration, executed October 10, 1996.

Oldham Declaration, executed October 10, 1996.

Spitler (Spitler I) Declaration, executed November 1, 1996.

Spitler (Spitler II) Declaration, executed August 25, 1997.

Spitler (Spitler III) Declaration, executed April 29, 1998.

(De Vita) CANCER: PRINCIPLES & PRACTICE OF ONCOLOGY 305 (De Vita et al., eds. 1993).

The rejections presented by the Examiner follow[1]:

1. Claims 1, 2, 4-8, 10-15, 17-22, 24-28, 30-34, and 37-40 stand rejected under 35 U.S.C. § 112, second paragraph.

2. Claims 1-14 and 21-40 stand rejected under the written description provision of 35 U.S.C. § 112, first paragraph.

3. Claims 1-14 and 21-40 stand rejected under the enablement provision of 35 U.S.C. § 112, first paragraph.

4. Claims 1-14 and 21-40 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Spitler '867, Israeli, Horoszewicz, Andriole, McCarley, and Appellants' admitted prior art taken alone or in further combination with Kuby, Paul, and Wright.

We reverse the rejection under 35 U.S.C. § 112, second paragraph. We affirm all other grounds of rejection.

Definiteness:

ISSUE

Is the term "over represented" indefinite in the context of Appellants' claimed invention?

FINDINGS OF FACT

FF 1. The Examiner finds that "the term 'over represented' is a relative term which renders the claims indefinite" (Ans. 24).

[1] The Examiner withdrew the rejection under the judicially-created doctrine of obviousness-type double patenting in view of Appellants' terminal disclaimers (Ans. 88).

FF 2. The Examiner finds that "[t]he term is not defined by the claim, the [S]pecification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention" (*id.*).

FF 3. Appellants' Specification discloses that the term "over represented" means

> that the concentration of this antigen in prostate is sufficiently higher than its concentration in any other tissue such that the prostate can effectively be targeted by the immune response raised against this antigen with relative sparing of other organs or tissues. Sparing can be measured by overall clinical toxicity to the subject. Toxicity to the subject is generally grade 3 or less, preferably grade 2 or less most preferably grade 1 or grade 0. The approach does not lose value with regard to metastatic prostate cancer, since the antigens overrepresented in the prostate gland are also carried by the metastatic cells.

(Spec. 5: 15-27; *see generally* Ans. 72.)

FF 4. Appellants' Specification further discloses that

> [K]nown antigens which are overrepresented on prostate: prostatic acid phosphatase (PAP); prostate specific antigen (PSA); and prostate specific membrane antigen (PSMA) . . . [are] offered for the purpose of illustration. These well known antigens (or the epitope bearing fragments thereof) are proteins (or peptides) and are useful in the vaccines of the invention. However, the invention includes any other antigens substantially uniquely present on the prostate gland so that prostate derived tissue can be distinguished from other tissue by virtue of the presence of these antigens.

(Spec. 9: 22 - 10: 2.)

PRINCIPLES OF LAW

Claim language must be analyzed "not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." *In re Moore*, 439 F.2d 1232, 1235 (CCPA 1971).

Claims are in compliance with 35 U.S.C. § 112, second paragraph, if "the claims, read in light of the specification, reasonably apprise those skilled in the art and are as precise as the subject matter permits." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385 (Fed. Cir. 1986).

ANALYSIS

Appellants' Specification defines the term "over represented" as the concentration of antigen in prostate that is sufficiently higher than its concentration in any other tissue such that the prostate can effectively be targeted by an immune response raised against the antigen with relative sparing of other organs or tissues (FF 3). Appellants' Specification makes clear that the term not only refers to those known antigens that are over represented in the prostate but also includes any other antigens that are substantially uniquely present on the prostate gland so that prostate derived tissue can be distinguished from other tissue by virtue of the presence of these antigens (FF 4).

When read in light of Appellants' Specification the term "over represented" as it appears in Appellants' claims reasonably apprise those skilled in the art and are as precise as the subject matter permits. *Hybritech,* 802 F.2d at 1385.

CONCLUSION OF LAW

The term "over represented" is not indefinite in the context of Appellants' claimed invention. The rejection of claims 1, 2, 4-8, 10-15, 17-22, 24-28, 30-34, and 37-40 under 35 U.S.C. § 112, second paragraph is reversed.

Written Description:

ISSUE

Have Appellants established that their Specification provides an enabling disclosure of prostate antigens other than the known PSA, PAP, and PSMA prostate antigens?

FINDINGS OF FACT

FF 5. Appellants' Specification discloses that

> [K]nown antigens which are overrepresented on prostate: prostatic acid phosphatase (PAP); prostate specific antigen (PSA); and prostate specific membrane antigen (PSMA) . . . [are] offered for the purpose of illustration. These well known antigens (or the epitope bearing fragments thereof) are proteins (or peptides) and are useful in the vaccines of the invention. However, the invention includes any other antigens substantially uniquely present on the prostate gland so that prostate derived tissue can be distinguished from other tissue by virtue of the presence of these antigens.

(Spec. 9: 22 - 10: 2.)

FF 6. Appellants' Specification discloses that

> The antigen can be any substance which is . . . unique to or overrepresented in prostate tissue. Thus, the antigen may be a protein or a peptide, or peptide fragment of the protein, or

> may be a carbohydrate, glycoprotein, lipoprotein or lipid. . . . Proteins may be modified by glycosylation or other derivatization. It is clear that in the case of protein antigen, peptides representing epitopes of the antigen may also be used.

(Spec. 6: 4-13.)

FF 7. The Examiner finds that Appellants' Specification fails to provide a description of "'over represented prostate antigens', including any 'protein[,] . . . peptide, . . . carbohydrate, glycoprotein, lipoprotein or lipid' other than those known prostate antigens at the time the invention was made, namely PSA, PAP and PSMA" (Ans. 11).

FF 8. The Examiner finds that Appellants failed to describe (1) the structural features commonly possessed by members of the genus of over represented prostate antigens that distinguish them from other antigens or (2) a correlation between the structure of the genus of over represented prostate antigens and their function "to induce an antitumor immune response for the prevention and treatment of prostatic cancer" (Ans. 31).

FF 9. The Examiner finds that six years after Appellants' filing date the only antigens Harris "identified that could serve as targets for an immune response" against prostate cancer were "PSA, PSMA and PAP" (Ans. 12).

PRINCIPLES OF LAW

> The "written description" requirement [under 35 U.S.C. § 112, first paragraph] implements the principle that a patent must describe the technology that is sought to be patented; the requirement serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed.

Capon v. Eshhar, 418 F.3d 1349, 1357 (Fed. Cir. 2005).

The written description must be of sufficient detail to show possession of the full scope of the invention. *Pandrol USA, LP v. Airboss Railway Products, Inc.*, 424 F.3d 1161, 1165 (Fed. Cir. 2005). When a genus is involved, the written description must define a genus to enable one skilled in the art to "visualize or recognize the identity of the members of the genus," e.g., by providing a description of "structural features commonly possessed by members of the genus that distinguish them from others." *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997).

> [T]he written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, *functional characteristics when coupled with a known or disclosed correlation between function and structure*, or some combination of such characteristics."

Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 964 (Fed. Cir. 2002). Stated differently, the written description "requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332 (Fed. Cir. 2003).

Arguments not made are waived. *See* 37 C.F.R. § 41.37(c)(1)(vii).

ANALYSIS

Appellants provide separate arguments for the following two Groups of claims: (I) claims 1-7 and (II) claims 8-14 and 21-40. Claims 1 and 8 are representative. Claims 37 C.F.R. § 41.37(c)(1)(vii).

Claim 1:

The subject matter of Appellants' claim 1 is drawn to a method to induce an antitumor immune response in a potential or actual prostate tumor-bearing subject. To achieve the stated purpose of the claimed method claim 1 requires the administration of a composition comprising an "*ingredient*," which is active to induce an immune response, to the potential or actual prostate tumor-bearing subject. The *ingredient* of claim 1 comprises either (1) at least one antigen over represented in the prostate gland or an immunologically effective portion thereof; or (2) an expression system capable of generating the antigen *in situ*.

Therefore, in order to accomplish the stated purpose of the method of claim 1, a person of ordinary skill in the art must have at least one antigen or immunologically effective portion thereof that is:

(1) over represented in the prostate gland and

(2) active to induce an immune response.

According to Appellants' Specification this antigen may be a protein, peptide, modified protein, carbohydrate, glycoprotein, lipoprotein, lipid, or any other antigen substantially uniquely present on the prostate gland so that prostate derived tissue can be distinguished from other tissue by virtue of the presence of these antigens (FF 5-6). The Examiner finds that Appellants' Specification fails to provide written descriptive support for the genus of antigens encompassed by the claim (FF 7-8).

Appellants disagree, contending that "the necessary common attribute of these antigens [is that] they are over represented on normal prostate tissue while also being expressed on malignant prostate tissue" (App. Br. 8). In this regard, Appellants contend that their Specification "discloses that the

concentration or representation of this antigen is sufficiently higher in normal prostate tissue relative to other normal tissues so that '*the prostate can be effectively targeted by the immune response raised against this antigen* with relative sparring of other organs or tissues" (*id.* (emphasis added)). Herein lies the problem.

The antigen required to perform the claimed method must not only be over represented in the prostate gland, but it must also be active to induce an immune response. While Appellants contend that the common attribute of the genus of antigens encompassed by claim 1 is that they are represented on both normal and malignant prostate tissue; Appellants fail to identify a disclosure in their Specification or prior art teaching that establishes a nexus between an antigens' over representation in the prostate gland (e.g., the common attribute) and the required activity of the antigen to induce an immune response (*see* FF 8).

While Appellants contend that PSA, PAP, and PSMA are representative of the genus encompassed by the claim (App. Br. 8-9), they fail to explain how these three antigens are representative of the genus comprising, *inter alia*, a carbohydrate, lipid, or other antigen that is encompassed by the method of claim 1 (FF 5-6).

We recognize Appellants' contention regarding "the use of known compounds" (App. Br. 9). However, Appellants failed to establish that with the exception of PSA, PAP, and PSMA, other antigens within the scope of the claimed genus where known in this art at the time the invention was made. As the Examiner points out, six years after Appellants' filing date the only antigens recognized in the art "that could serve as targets for an immune response" against prostate cancer were "PSA, PSMA and PAP" (FF

9). With the exception of PSA, PSMA, and PAP, Appellants failed to provide persuasive evidence or argument to support a conclusion that their Specification provides written descriptive support for the genus of prostate cancer antigens required to practice their claimed method.

Claim 8:

While Appellants' claim 8 is drawn to a pharmaceutical or veterinary vaccine for eliciting an antitumor immune response to prostate tumors in a subject, it suffers from the same deficiency as claim 1. Specifically, the lack of written descriptive support for an antigen that that is:

(1) over represented in the prostate gland and

(2) active to induce an immune response.

We recognize Appellants' contention that the genus of antigens encompassed by the composition of claim 8 "are sufficiently identified by their common necessary attribute" (App. Br. 11). While Appellants do not expressly state what this "common necessary attribute" is, it appears to be the same as that set forth for claim 1, specifically that they are represented on both normal and malignant prostate tissue. For the reasons set forth above, we are not persuaded by Appellants' contention.

CONCLUSION OF LAW

Appellants failed to establish that their Specification provides an enabling disclosure of prostate antigens other than the known PSA, PAP, and PSMA prostate antigens. The rejection of claims 1 and 8 under the written description provision of 35 U.S.C. § 112, first paragraph is affirmed.

Claims 2-7 fall together with claim 1. Claims 8-14 and 21-40 fall together with claim 8.

Enablement:

ISSUE

Have Appellants established that their Specification provides an enabling disclosure of prostate antigens other than the known PSA, PAP, and PSMA prostate antigens?

FINDINGS OF FACT

FF 10. The Examiner finds that Appellants' Specification provides an enabling disclosure of "'full-length PSA, PSMA and PAP'" (Ans. 16).

FF 11. The Examiner finds, however, that "the antigenic or immunogenic nature of a protein or expression system does not necessarily correlate with its ability to confer anti-tumor responses" (Ans. 17 (emphasis removed)).

FF 12. In this regard, the Examiner finds that

> As disclosed on page 2, paragraph 1 of the instant specification, [A]ppellant discloses that:
>
> "Prostate cancer continues to be refractory to treatment despite many years of efforts to improve therapy. Similarly, [A]ppellant discloses that at the time the invention was made; vaccine development has been slow and no vaccine approved by the FDA for marketing currently exists for any form of cancer."

(*Id.* (emphasis removed).)

PRINCIPLES OF LAW

Enablement is a question of law, based on underlying findings of fact. *See, e.g., In re Wands*, 858 F.2d 731, 735 (Fed. Cir. 1988). To satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, a patent application must adequately disclose the claimed invention so as to enable a person skilled in the art to practice the invention at the time the application was filed without undue experimentation. *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1371-72 (Fed. Cir. 1999). "[T]here must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed." *In re Vaeck*, 947 F.2d 488, 496 & n. 23 (Fed. Cir. 1991).

Arguments not made are waived. *See* 37 C.F.R. § 41.37(c)(1)(vii).

ANALYSIS

Appellants contend that the claims should be reviewed in the context of the following two Groups of claims: (I) claims 1-7 and (II) claims 8-14 and 21-40 (App. Br. 5-6). However, notwithstanding Appellants claim grouping, the only separate argument on this record regarding these two groups is that "Applicants submit that the patentability of the claimed methods of Group I lies in knowing what to do with the antigens, not in the identification of novel proteins or immunogenic peptides" (App. Br. 14). We disagree.

The issue in this case tests Appellants' disclosure against the scope of the claimed invention. More specifically the scope of the "antigen" required by both the method and composition claims.

Therefore, contrary to Appellants' contention that the issue does not involve the scope of the term antigen, the issue is precisely whether Appellants' Specification provides an enabling disclosure of prostate antigens other than the known PSA, PAP, and PSMA prostate antigens, regardless of whether these antigens are required to perform the claimed method (Group I) or as a constituent in the claimed composition (Group II). A claim must be enabled as broadly as it is claimed. Therefore, in short, the rejection before this panel is a scope of enablement rejection – relating to the scope of the antigen – which is required in both the method and composition.

Accordingly, since Appellants' sole argument relating to the separate patentability of the claims applied to both of Appellants' claim groupings we limit our discussion to representative claim 1. Claims 2-14 and 21-40 will stand or fall together with claim 1. Claims 37 C.F.R. § 41.37(c)(1)(vii).

The Examiner finds that Appellants' Specification provides an enabling disclosure of "'full-length PSA, PSMA and PAP'" (FF 10). Thus, the issue before this panel is whether Appellants' Specification provides an enabling disclosure of prostate antigens other than the known PSA, PAP, and PSMA prostate antigens.

Appellants' Specification discloses that the antigen required by claim 1 may be any antigen "substantially uniquely present on the prostate gland so that prostate derived tissue can be distinguished from other tissue by virtue of the presence of these antigens" (FF 5), including protein, modified protein, peptide, carbohydrate, glycoprotein, lipoprotein, and lipid (FF 6). Appellants contend that PSA, PSMA, and PAP are representative of the foregoing genus of structurally and biochemically distinct antigens (App. Br.

13). Specifically, Appellants contend that "[t]he specification provides three representative examples in the genus of over represented antigens, *i.e.*, PSA, PSMA, and PAP as well as an explicit, specific definition for the genus" (*id.*). Appellants define this genus as those antigens "that are substantially uniquely present on the prostate gland so that prostate derived tissue can be distinguished from other tissue by virtue of the presence of these antigens and that can serve as a target for an immune response with relative sparring of other organs or tissues" (*id.*).

Accordingly, Appellants appear to suggest that simply because an antigen is over represented on the prostate it will necessarily be active to induce an immune response in a potential or actual prostate tumor-bearing subject. In this regard, Appellants contend that "[o]ne of skill in the art would recognize these antigens as host antigens, i.e., expressed on normal tissue, whose expression level is a distinguishing feature of prostate tissue and therefore allows a targeted immune response to eliminate the prostate tissue (normal and malignant) with relative sparring of other tissues" (*id.*).

However, as the Examiner points out "the antigenic or immunogenic nature of a protein or expression system does not necessarily correlate with its ability to confer anti-tumor responses" (FF 11; *see also* FF 12). In further support of this reasoning, the Examiner finds that six years after Appellants' filing date the only antigens recognized in the art "that could serve as targets for an immune response" against prostate cancer were "PSA, PSMA and PAP" (FF 9). Accordingly, we disagree with Appellants' contention that "[t]he antigens are sufficiently identified as antigens substantially uniquely expressed on prostate tissue to inform the skilled artisan of their identity" (App. Br. 13). To the contrary, even if a person of ordinary skill in the art

could identify antigens, other than PSA, PSMA, and PAP, that are over represented in the prostate gland; there is no expectation that such an antigen would be active to induce an antitumor immune response. On this point, the evidence on this record weighs in favor of the Examiner.

We recognize Appellants' contention that "[a]ny experimentation that is required to practice the claimed methods is routine" (*id.* at 14). In this regard, Appellants contend that the patentability of their claim "lies in knowing what to do with the antigens, not in the identification of novel proteins or immunogenic peptides" (*id.*). Appellants rely on the Livingston, Bystryn, Mastrangelo, and Oldham Declarations to support their contentions (*id.*).

Each of these declarations address a "Declaration Under 37 C.F.R. 1.132 prepared by Dr. Lynn E. Spitler describing the results of a clinical study directed to the use of prostate specific antigen (PSA) as an active ingredient in an antiprostate cancer vaccine" (Livingston Dec. 1-2: ¶ 2; Bystryn Dec. 1: ¶ 2; Mastrangelo 1: ¶ 2; and Oldham 1: ¶ 2). Each of these Declarant's concludes that PSA based "vaccines are likely to be effective in exerting a beneficial effect on patients with prostate tumors or at risk for prostate tumors" and that vaccines based on PSMA and PAP "would behave in a similar manner" (Livingston Dec. 2-3: ¶¶ 5-6; Bystryn Dec. 2: ¶¶ 5-6; Mastrangelo 2: ¶¶ 5-6; and Oldham 2: ¶¶ 5-6).

Each of these Declarations address the three antigens that the Examiner has expressly stated are enabled by Appellants' Specification (FF 10). Claim 1 is not, however, limited to these three antigens; nor is it limited to proteins or peptides. Instead, the claim encompasses any antigen "substantially uniquely present on the prostate gland so that prostate derived

tissue can be distinguished from other tissue by virtue of the presence of these antigens" (FF 5), including protein, modified protein, peptide, carbohydrate, glycoprotein, lipoprotein, and lipid (FF 6).

Appellants have failed to identify a disclosure in their Specification, teaching in the art, or Declaratory evidence that suggests that a person of ordinary skill in this art would have reasonably expected an antigen would be capable of inducing an antitumor immune response simply because it is over represented in the prostate gland. Accordingly, notwithstanding Appellants' contention to the contrary, the evidence of record fails to support Appellants' contention that undue experimentation would not be required to identify an antigen that exhibits the property of inducing an antitumor immune response that is within the scope of Appellants' claim 1, other than PSA, PSMA and PAP.

For the foregoing reasons we are not persuaded by Appellants' reliance on the Spitler III Declaration which, "uses one of the species in the claimed genus of over represented antigens on prostate cancer, namely PSA," to support a conclusion that their Specification provides an enabling disclosure that is commensurate in scope with claim 1 (App. Br. 15). As Appellants concede, "the PSA in the vaccine used by Spitler is a protein" (*id.* at 16). There is no persuasive evidence or argument on this record to support a conclusion that a person of ordinary skill in this art at the time this invention was made would expect the results obtained with PSA would have been representative of structurally and biochemically distinct antigens, such as a lipid or carbohydrate, that are encompassed within the scope of claim 1. In this regard, we disagree with Appellants' contention that the Examiner "has given the declaration no weight whatsoever" (*id.*). To the contrary, the

Examiner has acknowledged that Appellants' Specification provides an enabling disclosure of the PSA antigen (FF 10). The Examiner's concern, however, is the basis for Appellants' extrapolation of the results obtain for PSA to any other antigen, including those that may be structurally and biochemically distinct from PSA, that may be over represented in prostate.

We recognize Appellants' reliance on the Spitler I Declaration to support the conclusion that "[a] skilled artisan does not equate cell-based vaccines with purified antigen-based vaccines" (App. Br. 17). The Spitler I Declaration does not, however, address the Examiner's concern with regard to the failure of Appellants' Specification to provide an enabling description commensurate in scope with claim 1. Accordingly, we are not persuaded by Appellants' reliance on the Spitler I Declaration.

CONCLUSION OF LAW

Appellants failed to establish that their Specification provides an enabling disclosure of prostate antigens other than the known PSA, PAP, and PSMA prostate antigens.

The rejection of claims 1 and 8 under the enablement provision of 35 U.S.C. § 112, first paragraph is affirmed.

Claims 2-7 fall together with claim 1. Claims 8-14 and 21-40 fall together with claim 8.

Obviousness:

ISSUE

Have Appellants established error in the Examiner's conclusion that Appellants' claimed invention is prima facie obvious?

FINDINGS OF FACT

FF 13. Office records establish that the instant Application is a continuation of Application No. 09/300,978. The 09/300,978 Application was involved in Appeal No. 2004-1185.

FF 14. Claim 13 was representative of the subject matter in Appeal No. 2004-1185 and is reproduced below:

> 13. A method to elicit an antitumor immune response to prostate tumors in a subject, which methods comprises
> administering to said subject at least one active ingredient formulated for administration to said subject,
> wherein said active ingredient comprises or expresses at least one antigen over-represented in the prostate gland,
> wherein said antigen is human prostate-specific membrane antigen (PSMA); or
> prostatic acid phosphatase (PAP); or mixtures of the foregoing; or
> wherein said active ingredient comprises said at least one antigen or nucleic acid that generates said antigen or antigens in situ .

(Decision on Appeal No. 2004-1185: 2.)

FF 15. The Examiner has not disputed on this record, nor in the record of Appeal No. 2004-1185 "that the effective filing date of the claims on appeal is August 11, 1993" (Decision on Appeal No. 2004-1185: 5).

FF 16. While the Examiner asserts that Kuby has a 1991 publication date (Ans. 27; Kuby acknowledges the "Cover credits" as having a 1991 copyright date. Kuby's actual publication date is 1994 (*see* copyright data page for Kuby's bibliographic data). Accordingly, Kuby is not available as prior art against Appellants' claimed invention (*see* Decision on Appeal No. 2004-1185: 5).

FF 17. As found by the earlier Decision, "Spitler describes antitumor vaccine compositions and methods for treating tumors. Specifically, the method described by Spitler employs liposome compositions that encapsulate or are conjugated to tumor associated antigens (TAAs) or antiidiotypic monoclonal antibodies (anti-ids) to TAAs" (Decision on Appeal No. 2004-1185: 5).

FF 18. "A TAA is an antigen that is expressed on tumor cells and normal cells during at least some stage of differentiation" (*id.* at 7).

FF 19. While Spitler teaches the use of e.g., GA733-2, which

> is associated with a number of organs including the prostate, the [E]xaminer has not asserted that GA733-2 is an antigen that is over-represented in the prostate gland as is PSMA. Rather, the [E]xaminer's position is that PSMA would be considered a TAA by a person of ordinary skill in the art at the time of the present invention and thus, that hypothetical person would have found it obvious to use PSMA in the antitumor method described in Spitler.

(*id.* at 6.)

FF 20. "[B]oth Horoszewicz and Israeli describe PSMA," which is over-represented in the prostate gland and "meets the definition of TAA set forth in Paul" (*id.* at 7).

FF 21. The previous Decision framed the issue as follows: "[W]ould it have been obvious to a person of ordinary skill in the art at the time of the present invention to use PSMA in the anti-tumor vaccine described by Spitler?" (*Id.* at 8.)

FF 22. The panel in the prior Decision then concluded that "it is reasonable to conclude that a vaccine based upon PSMA itself instead of anti-ids to PSMA would be effective against prostatic tumors" (*id.*).

PRINCIPLES OF LAW

"[T]he [E]xaminer bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability." *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992). On appeal to this Board, Appellants must show that the Examiner has not sustained the required burden. *See Ex parte Yamaguchi*, 88 USPQ2d 1606, 1608 and 1614 (BPAI 2008) (precedential); *Ex parte Fu*, 89 USPQ2d 1115, 1118 and 1123 (BPAI 2008) (precedential).

"The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). It is proper to "take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at 418. *See also id.* at 421 ("A person of ordinary skill is also a person of ordinary creativity, not an automaton."). In sum, the "suggestion test is in actuality quite flexible and not only permits, but *requires*, consideration of common knowledge and common sense." *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1367 (Fed. Cir. 2006).

> [C]ase law does not require that a particular combination must be the preferred, or the most desirable, combination described in the prior art in order to provide motivation for the current invention. "[T]he question is whether there is something in the prior art as a whole to suggest the *desirability*, and thus the obviousness, of making the combination," not whether there is something in the prior art as a whole to suggest that the combination is the *most desirable* combination available. . . . [A] finding that the prior art as a whole suggests the desirability of a particular combination need not be supported by a finding that the prior art suggests that the combination claimed by the

> patent applicant is the preferred, or most desirable, combination.

In re Fulton, 391 F.3d 1195, 1200 (Fed. Cir. 2004) (internal citations omitted).

"[A] reference may teach away from a use when that use would render the result inoperable." *In re ICON Health and Fitness, Inc.*, 496 F.3d 1374, 1381 (Fed. Cir. 2007).

"[A] Board decision in an application is the 'law of the case,' and is thus controlling in that application and any subsequent, related application" Manual of Patent Examining Practice § 706.07(h)(XI)(A), 8th ed., Rev. 6, September 2007.

Arguments not made are waived. *See* 37 C.F.R. § 41.37(c)(1)(vii).

ANALYSIS

Appellants contend that the claims should be reviewed in the context of the following two Groups of claims: (I) claims 1-7 and (II) claims 8-14 and 21-40 (App. Br. 6). In this regard, Appellants contend that "the references do not teach or suggest the use of over represented prostate antigens in a subject to elicit an active antitumor response [(claims 1-7)] or the vaccine compositions comprising over represented prostate antigens" (claims 8-14 and 21-40) (App. Br. 24). Claims 1 and 8 are representative. Claims 37 C.F.R. § 41.37(c)(1)(vii).

Claims 1 and 8:

Appellants' arguments regarding claims are presented together. Accordingly, we address both of these claims in the manner presented by Appellants.

Appellants contend that "Spitler discloses the use of antigens (*i.e.*, CO-029 and GA733-2) that are each characterized by expression on multiple types of malignant cells" (App. Br. 25). Accordingly, Appellants contend that "Spitler does not teach the use of the over represented prostate antigens in vaccine compositions of Group II or the methods of Group I" (*id.*). We are not persuaded.

> While Spitler teaches the use of e.g., GA733-2, which
>
> is associated with a number of organs including the prostate, the [E]xaminer has not asserted that GA733-2 is an antigen that is over-represented in the prostate gland as is PSMA. Rather, the [E]xaminer's position is that PSMA would be considered a TAA by a person of ordinary skill in the art at the time of the present invention and thus, that hypothetical person would have found it obvious to use PSMA in the antitumor method described in Spitler.

(FF 19; *see also* Decision on Appeal No. 2004-1185: 8-9 ("[w]e agree, as did the [E]xaminer, that the two specific antigens discussed in Spitler . . . are not antigens over represented in the prostate gland. . . . However, [A]ppellants' argument overlooks the broader disclosure in Spitler of using TAAs in general"); *See* FF17.)

Appellants contend that since passive immunotherapy is recognized in the art to be distinct from active immunotherapy (App. Br. 26-27), "the ability to generate antibodies to PSMA or the suggestion to use such antibodies in passive immunotherapy has no relevance to the instant claims

drawn to methods and compositions of active immunotherapy of prostate cancer" (App. Br. 27). In this regard, Appellants contend that "Horoszewicz's only disclosure of an active immunotherapy protocol does not employ antigen, but uses anti-idiotype antibodies, a fundamentally different therapy (*i.e.,* antigen administration is never required)" (*id.*). We are not persuaded.

Notwithstanding Appellants' contention to the contrary, Spitler teaches the use of either antigen or antiidiotypic antibodies in antitumor vaccine compositions (FF 17; *see also* Ans. 85 ("Spitler . . . teaches that their invention may employ either tumor associated antigens or anti-idiotypic antibodies to tumor associated antigens . . . for the treatment of a variety of cancers"); and Decision on Appeal No. 2004-1185: 9 ("Spitler itself states that either therapy, i.e., use of an antigen or an anti-id, will work in the tumor vaccines of that reference")). Accordingly, we disagree with Appellants' contention that "[b]ecause . . . Horoszewicz do not teach the use of the prostate antigens in active immunotherapy, . . . [the] reference alone or in combination with Spitler teach the instant claimed inventions" (App. Br. 27). Instead, "it is reasonable to conclude that a vaccine [or method of using such a vaccine] based upon PSMA itself instead of anti-ids to PSMA would be effective against prostatic tumors" (FF 22).

Appellants contend that the Examiner acknowledges that "Andriole actually teaches away from the need for immunotherapy" by "stating that Andriole teaches that 'surgical excision of the prostate is unsurpassed as a means of controlling organ-confined prostate cancer" (App. Br. 28). We disagree. "'[T]he question is whether there is something in the prior art as a whole to suggest the *desirability*, and thus the obviousness, of making the

combination,' not whether there is something in the prior art as a whole to suggest that the combination is the *most desirable* combination available." *Fulton*, 391 F.3d at 1200.

Appellants contend that Spitler teaches away from the claimed methods and composition by teaching vaccines that are effective in the treatment of a variety of cancers and that "[a] skilled artisan would recognize that the administration of a prophylactic vaccine that elicits an immune response to an antigen on normal tissues would result in autoimmunity specific for that tissue, a potentially fatal side effect" (App. Br. 28-29; *Cf.* Decision on Appeal No. 2004-1185: 9). However, as set forth in the Decision on Appeal No. 2004-1185:

> [T]his argument again loses sight of the broader description in Spitler of using TAAs in general and the specific disclosure of Horoszewicz and Israeli in regard to PSMA. While the two specific TAAs discussed in Spitler may very well be useful in treating a variety of tumors, it is equally clear that immunotherapy of prostatic cancer based upon PSMA would be specific to prostatic tissue whether normal or malignant as discussed in Horoszewicz and Israeli. Furthermore, since PSMA is specific to the prostate gland, its use in an antitumor vaccine would not be expected to harm other tissues. Destruction of the prostate gland would not be considered a potentially fatal side effect.

(*Id.* at 9-10.) Accordingly, we are not persuaded by Appellants' contentions to the contrary.

Lastly, for the reasons set forth at page 8 of the Decision on Appeal No. 2004-1185, we are not persuaded by Appellants' contention that "the references do not provide a reasonable expectation of success in any combination" (App. Br. 29).

CONCLUSION OF LAW

Appellants failed to establish error in the Examiner's conclusion that Appellants' claimed invention is prima facie obvious.

We affirm the rejection of claims 1 and 8 under 35 U.S.C § 103(a) as unpatentable over the combination of Spitler '867, Israeli, Horoszewicz, Andriole, McCarley, and Appellants' admitted prior art taken alone or in further combination with Paul and Wright. Claims 2-7 fall together with claim 1. Claims 9-14, and 21-40 fall together with claim 8.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

cdc

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